VERSION OF APPLICATION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

At page 1, replace the paragraph beginning at line 3 with the following:

The invention lies in the field of nucleic acid cross-linking and uses thereof. More specifically the invention relates to methods for producing selected interstrand cross-links in nucleic acids and uses thereof. One important aspect of the invention relates to the use of selected interstrand cross-links for the selective amplification of certain nucleic acids in an amplification reaction.

Replace the paragraph bridging pages 1 and 2 with the following:

Many different compounds have been identified that ~~posses~~ possess nucleic acid cross-linking activity. Cross-linking of nucleic acids is most commonly used for therapeutic purposes in the intervention with proliferative disorders such as cancer. Most cross-linking agents cross-link nucleic acids in very specific ways and on specific places in nucleic acids. However, the frequency of these specific places in most nucleic acids are so high that effectively the cross-links are provided throughout the nucleic acid molecules. For the use of these cross-linking compounds in the intervention of cancer this so-called apparently random cross-linking activity does not prevent some kind of therapeutic effect. However, in the ideal situation cross-links would only be applied in the nucleic acid of the cells of which the proliferation should be interfered with. For instance by applying cross-links only to those nucleic acids involved in the transformation of said cell, i.e. the oncogenes or the RNA of said oncogenes. Such specificity was not possible with the current methods of cross-linking. The apparent random cross-linking activity of cross-linking agents also prevents the use of these compounds in assays that require more specific cross-linking. In one aspect the invention provides a method for producing cross-links in selected regions of a nucleic acid.

In one aspect said method may be used to prevent at least in part, certain regions in a nucleic acid from taking part in a process such as, but not limited to, a process comprising a hybridisation or an amplification or both. In one aspect said method of producing selected interstrand cross-links is used in a process for producing a probe deprived at least in part of repetitive sequences. Such a probe is useful for the detection of for example nucleic acid sequences in chromosome painting in the field of cytogenetics.

At page 11, replace the paragraph beginning at line 6 with the following:

Some labelled chromosomes or parts thereof may be used for the typing of a chromosome and/or cell or for the identification of a disease.~~0000~~

IN THE CLAIMS:

Please cancel Claims 13-15.

Please add Claims 24-33.

24. (New) A method for distinguishing at least two target bio-organic molecules with dyes selected from a pool of at least two dyes, the method comprising:

(a) providing a first set of at least two probes, wherein each probe recognizes a target bio-organic molecule in a first set of target bio-organic molecules, and wherein each probe is distinctly-labelled with primary labels that are distinct from one another due to the presence of dyes in distinct ratios;

(b) providing a second set of probes distinctly-labelled with said primary labels described in step (a), wherein each probe in said second probe set recognizes a target bio-organic molecule in a second set of target bio-organic molecules;

wherein each probe in said first or second probe set is further labelled with the same first binary label, wherein said first binary label is distinct from said primary labels; and

(c) contacting said at least two target bio-organic molecules with said probe sets,

wherein said target bio-organic molecules are distinguished.

25. (New) A method according to Claim 24 further providing an additional probe set distinctly labelled with said primary labels, wherein each probe in said additional probe set recognizes target bio-organic molecule(s) in an additional target set, and wherein each probe in said additional set is further labelled with the same second binary label, wherein said second binary label is distinct from said primary labels and said first binary label.

26. (New) A method according to Claim 24 wherein said primary labels are distinct from one another due to the presence of two dyes in distinct ratios.

27. (New) A method according to Claim 24, wherein at least one of said bio-organic molecules comprises a nucleic acid, protein, carbohydrate and/or lipid.

28. (New) A method according to Claim 24, wherein said pool comprises three dyes.

29. (New) A method according to Claim 24, wherein said labelling comprises nick translation, random primed labelling, PCR-labelling or chemical labelling.

30. (New) A method according to Claim 24 wherein said binary label is a hapten.

31. (New) A method for labelling at least two probes with dyes selected from a pool of at least two dyes, wherein said labelled probes are distinguishable from one another, the method comprising:

(a) distinctly labelling with primary labels a first set of at least two probes, wherein each probe recognizes a target bio-organic molecule in a first set of target bio-organic molecules, and wherein said primary labels are distinct from one another due to the presence of dyes in distinct ratios; and

(b) distinctly labelling a second set of probes with said primary labels described in step (a), wherein each probe in said second probe set recognizes a target bio-organic molecule in a second set of target bio-organic molecules; and

(c) labelling each probe in said first or second probe set with a binary label, wherein said binary label is distinct from said primary labels, and wherein each probe in said first or second set is labelled with the same binary label;

wherein said probes are labelled.

32. (New) A kit for labelling at least two bio-organic molecules, comprising:

(a) a first set of probes wherein each probe in said set recognizes a target bio-organic molecule in a first set of target bio-organic molecules, wherein each probe in said first probe set is distinctly-labelled with primary labels, and wherein said primary labels are distinct from one another due to the presence of dyes in distinct ratios; and

(b) a second set of probes distinctly-labelled as described in step (a), wherein each probe in said second probe set recognizes a target bio-organic molecule in a second set of target bio-organic molecules; and wherein said second probe set is further labelled with a binary label which is distinct from the labels used in step (a).

33. (New) A kit according to Claim 32 further comprising additional set(s) of probes distinctly-labelled with said primary labels, wherein each probe in said additional probe set(s) recognizes target bio-organic molecules in additional target set(s), and wherein said

additional probe set(s) are further labelled with binary labels which are distinct from the labels used in Claim 31, and distinct from one another.